Table 7. Advantages and Disadvantages of Antiretroviral Components Recommended as Initial Antiretroviral Therapy

ARV Class	Antiretroviral Agent(s)	Advantages	Disadvantages
NNRTIs		**NNRTI Class Advantages:** • Less fat maldistribution and dyslipidemia than PI-based regimens • Save PI options for future use	**NNRTI Class Disadvantages:** • Low genetic barrier to resistance (single mutation confers resistance) • Cross resistance among NNRTIs • Skin rash • Potential for CYP450 drug interactions (See Tables 19-21b)
	Efavirenz (preferred NNRTI)	• Potent antiretroviral activity • Low pill burden and frequency (1 tablet per day)	• Neuropsychiatric side effects • Teratogenic in nonhuman primates, contraindicated in 1st trimester of pregnancy and avoid use in women with pregnant potential
	Nevirapine	• No food effect • No evidence of increase adverse hepatic events in women who received single dose nevirapine for prevention of mother to child transmission (PMTCT)	• Higher incidence of rash than with other NNRTIs, including rare but serious hypersensitivity reactions (Stevens-Johnson Syndrome or toxic epidermal necrolysis) • Higher incidence of hepatotoxicity than with other NNRTIs, including serious and even fatal cases of hepatic necrosis • Female patients and patients with high pre-NVP $CD4^+$ T cell counts (>250 cells/mm^3 in females & >400 cells/mm^3 in males) are at a higher risk of symptomatic hepatic events. NVP is not recommended in these patients unless the benefit clearly outweighs the risk.
PIs		**PI Class Advantage:** • Save NNRTI for future use • Longest prospective study data including data on survival benefit	**PI Class Disadvantages:** • Metabolic complications - fat maldistribution, dyslipidemia, insulin resistance • CYP3A4 inhibitors & substrates – potential for drug interactions (more pronounced with ritonavir-based regimens) (See Tables 19-21b)
	Lopinavir/ ritonavir (preferred PI)	• Potent antiretroviral activity • Co-formulated as Kaletra® • Potential for once daily dosing in treatment-naïve patients • No food restriction with oral tablet formulation	• Gastrointestinal intolerance (higher incidence with once daily than twice daily dosing) • Hyperlipidemia • Preliminary data show lower drug exposure in pregnant women
	Atazanavir	• Less adverse effect on lipids than other PIs • Once daily dosing • Low pill burden (2 pills per day)	• Indirect Hyperbilirubinemia • PR interval prolongation – generally inconsequential unless combined with another drug with similar effect • Reduced drug exposure when used with tenofovir and efavirenz – avoid concomitant use unless combined with RTV (ATV 300mg qd + RTV 100mg qd) • Absorption depends on food and low gastric pH
	Fosamprenavir	• Lower pill burden than amprenavir (4 vs. 16 cap per day) • No food effect	• Skin rash
	Fosamprenavir/ Ritonavir	• Lower pill burden than amprenavir/ritonavir • Once daily regimen in patients with no history of PI failure • No food effect	• Skin rash
	Indinavir/ ritonavir	• RTV-boosting allows for twice-daily instead of 3-times-daily dosing • Eliminates food restriction of indinavir	• Potential for higher incidence of nephrolithiasis than with IDV alone • High fluid intake required (1.5–2 liters of fluid per day)
	Nelfinavir	• Favorable safety and pharmacokinetic profile for pregnant women when compared to other PIs	• Diarrhea • Higher rate of virologic failure when compared to other PIs (LPV/r & fosamprenavir) and efavirenz in clinical trials • Food requirement
	Saquinavir (hgc, sgc, or tablets) + ritonavir	• Low-dose ritonavir reduces saquinavir daily dose and frequency	• Gastrointestinal intolerance (hgc or tablets better tolerated than sgc)

Table 7. Advantages and Disadvantages of Antiretroviral Components Recommended as Initial Antiretroviral Therapy

ARV Class	Antiretroviral Agent(s)	Advantages	Disadvantages
NRTIs		• Established backbone of combination antiretroviral therapy	• Rare but serious cases of lactic acidosis with hepatic steatosis reported with most NRTIs
Triple NRTI regimen	Abacavir + zidovudine + lamivudine only	• Abacavir + zidovudine + lamivudine - Co-formulated as Trizivir® • Minimal drug-drug interactions • Low pill burden • Saves PI & NNRTI for future use	• Inferior virologic response when compared to efavirenz-based and indinavir-based regimens • Potential for abacavir hypersensitivity reaction
Dual NRTIs: backbone of three or more drug combination therapy	Zidovudine + lamivudine	• Most extensive and favorable virological experience • Co-formulated as Combivir®– ease of dosing • No food effect • Lamivudine – minimal side effects	• Bone marrow suppression with zidovudine • Gastrointestinal intolerance
	Stavudine + lamivudine	• No food effect	• Peripheral neuropathy, lipoatrophy, hyperlactatemia and lactic acidosis, reports of progressive ascending motor weakness, potential for hyperlipidemia with stavudine use • Stavudine - Higher incidence of mitochondrial toxicity than with other NRTIs
	Tenofovir + lamivudine	• Good virologic response when used with efavirenz • Once-daily dosing • No food effect	• Tenofovir – some reports of renal impairment • Interactions with: 1. atazanavir – tenofovir reduces atazanavir levels – need to add ritonavir); and 2. didanosine – tenofovir increases didanosine level – need to reduce dose of didanosine
	Abacavir + lamivudine	• No food effect • Study showing non-inferior to zidovudine + lamivudine as 2-NRTI backbone • Once daily dosing • Co-formulation (Epzicom®)	• Potential for abacavir systemic hypersensitivity reaction • Higher incidence of severe hypersensitivity reactions with once daily dosing as compared to twice daily dosing of Abacavir reported in one study
	Didanosine + lamivudine	• Once-daily dosing	• Peripheral neuropathy, pancreatitis – associated with didanosine • Food effect – needs to be taken on an empty stomach • Requires dosing separation from most PIs • Potential increase in toxicities when used with ribavirin, tenofovir, or hydroxyurea (lower dose of didanosine is recommended when used with tenofovir)
	NRTI + emtricitabine (in place of lamivudine)	• Long half-life than lamivudine • Once daily dosing • Co-formulation with tenofovir (Truvada®)	• Less experience than lamivudine